FOLFIRI. **CONCLUSIONS:** FOLFOX appears to have favorable cost effectiveness compared to other agents in the treatment of stage IV colorectal cancer, even after factoring in the impact of generic irinotecan.

PODIUM SESSION I: DRUG UTILIZATION STUDIES

DU1

PHYSICAL FUNCTION AND THE CONCOMITANT USE OF ANTICHOLINERGIC ANTIHISTAMINES AND CHOLINESTERASE INHIBITORS AMONG MEDICAID RECIPIENTS WITH DEMENTIA

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OBJECTIVES: Antihistamines with anticholinergic properties (AA) are often used to treat comorbidities in patients with dementia. Use of AA with cholinesterase inhibitors (CHI) may counteract benefits of CHI in improving activities of daily living (ADL) or slowing ADL decline. Associations between use of AA with CHI and ADL function were assessed. **METHODS:** A retrospective cohort analysis of Indiana Medicaid claims and enrollment data from July 2001 through December 2005 merged with Minimum Data Set (MDS) identified persons ≥65 years, with dementia based on previously assessed criteria for identifying dementia and, receiving CHI. Persons taking anticholinergics other than AA during the study interval from first to last MDS assessment during CHI use were excluded. Piecewise repeated measures analysis used days taking AA and days not taking AA during each assessment interval as predictors to estimate influence of AA use on MDS ADL function scores (range 0–28, higher scores = more dependence). Presence of shifts in curves and changes in slopes defined changes in ADL. Age, gender, race, region, marital status and number of medications taken at the start of CHI use, Charlson comorbidity score and propensity score for receipt of AA were included as fixed covariates. **RESULTS:** A sample of 2,690 persons with mean age of 82 years, 75% female and, 90% white was identified. Of these, 691 (26%) used AA. Overall, a 0.45 ($p = 0.02$) upward shift in ADL score indicated an immediate decrease in ADL function with AA use. Among persons with moderate ADL dependence (score 6–12), an increase in slope of 0.53 ($p = 0.04$) per quarter also was observed indicating faster decline with AA use. **CONCLUSIONS:** Use of AA with CHI is associated with greater ADL decline in Medicaid recipients with dementia. Potential impact of AA use on physical function should be considered before prescribing AA with CHI.

DU2

RACIAL DIAPARITIES AND BARRIER TO DRUG UTILIZATION IN PATIENTS WITH DIABETES IN THE UNITED STATES

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OBJECTIVES: We sought to assess barriers to the appropriate statin usage measured through out-of-pocket payment by insurance status and racial disparities in patients with diabetes. **METHODS:** We analyzed 1,708 civilian, non-institutionalized patients with diabetes aged between 20 and 85 in the 2003 Medical Expenditure Panel survey (MEPS), a nationally representative survey in the United States which was linked to drug utilization files. We categorized patients with diabetes into six mutually exclusive insurance groups. We performed bivariate chi-square tests to assess the association between race and statins use, and insurance status and statin use during the year. We further performed multivariate logistic regression analysis to assess the effect of race/ethnicity on statin usage for patients of different races/ethnicity, controlling for socioeconomic variables, and co-morbid conditions. **RESULTS:** Among the population, 369 (21.6%) were African American, 66 (3.9%) Asian and 396 (23.2%) were Hispanic; the mean out-of-pocket payment per prescription of statins was $61.4 (SD $62.5) for Medicare patients, $24.0 (SD $43.7) for Medicaid patients, $ 25.4 (SD $49.0) for patients with dual eligibility, $35.2 (SD $33.5) for those with private insurance, $76.7 (SD $47.8) for those without insurance, and $83.9 (SD $90.5) for others. In bivariate analysis, statin usage was found to be significantly different across races and insurance status ($p = 0.020$ and $p < 0.0001$, respectively). In multivariate regression analysis, compared to White patients, African American patients were less likely to use statin (adjusted OR 0.57, 95% CI 0.43–0.76, $p < 0.0001$). Asian and Hispanic patients were marginally less likely to use statin (adjusted OR 0.60, 95% CI 0.34–1.05, $p = 0.078$; and adjusted OR 0.75, 95% CI 0.56–1.00, $p = 0.055$, respectively). **CONCLUSIONS:** Drug utilization is associated with insurance coverage. Racial/ethnicity disparity is observed in drug utilization of patients with diabetes after adjusting for insurance status.

DU3

PATTERN OF UTILIZATION OF PEGFILGRASTIM IN PATIENTS WITH CHEMOTHERAPY-INDUCED NEUTROPENIA: A RETROSPECTIVE ANALYSIS OF ADMINISTRATIVE CLAIMS DATA

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OBJECTIVES: Pegfilgrastim is a long-acting granulocyte colony-stimulating factor (G-CSF) used to prevent or treat febrile neutropenia associated with myelosuppressive anticancer therapies. According to the prescribing information, pegfilgrastim should not be administered within 14 days before or 24 hours after cytotoxic chemotherapy because of the potential for myeloid toxicity. This study examined use patterns of pegfilgrastim in real-life practice. **METHODS:** Analysis of health insurance claims data in 2000–2007 from >35 large health plans across the US was conducted. Patients who had a cancer diagnosis and chemotherapy within 120 days of their first pegfilgrastim injection were identified. The proportion of pegfilgrastim injections that were followed by administration of chemotherapy within 11 and 9 days was calculated. Analysis was also stratified by cancer type [Non-Hodgkin's lymphoma (NHL), lung, and breast]. **RESULTS:** A total of 13,526 cancer patients received 57,118 pegfilgrastim injections. NHL, lung, and breast cohorts comprised 2,722, 2,772, and 4,955 patients, respectively. Mean age (SD) was 55.0 (11.6) and women represented 65.9% of study population. Among all cancer types, 19.2% of pegfilgrastim injections had a chemotherapy claim within the following 11 days. This pattern of use was the highest in NHL (18.9%), followed by lung (17.1%), and breast (16.2%). Similar results were observed in the 9-day sensitivity analysis (all cancer: 16.2%, NHL: 17.4%, lung: 16.0%, breast: 14.7%). **CONCLUSIONS:** Based on the retrospective analysis of this administrative claims database, the use of pegfilgrastim within 11 days of an administration of chemotherapy was observed in 15–20% of cases which is inconsistent with the recommended guidelines. Pegfilgrastim use in these situations may have the potential to increase sensitivity of rapidly dividing myeloid cells to cytotoxic chemotherapy. Further research is being conducted to assess the related clinical and economic impact of this pattern of usage.

(For DU4 see page A185)

DU4

PODIUM SESSION I: PERSONALIZED MEDICINE

PM1

PERSONALIZED MEDICINE: FACTORS INFLUENCING REIMBURSEMENT

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OBJECTIVES: Personalized medicine (PM) has attracted tremendous interest, but yielded few marketed products. We examined factors influencing the approval, coverage, and reimbursement of existing PM technologies. **METHODS:** We conducted six case studies of paired genetic tests and treatments in order to develop a framework to explain differences in adoption and reimbursement. We divided these case studies into three groups based on the purpose of the PM technology: Disease differentiation (HER2/neu with Herceptin (trastuzumab), hepatitis C genotyping with ribavirin/pegylated interferon, and Oncotype DX with chemotherapy); pharmacogenetics (UGT1A1 with irinotecan (Camptosar) and VKORC1/CYP2C9 with warfarin) and predisposition tests (BRCA 1/2 with prophylactic surgical measures and Oncotype DX with chemotherapy). **RESULTS:** The factors influencing approval, coverage and reimbursement appear based broadly on the purpose of, and evidence for, the PM technology, rather than the type of device regulation (i.e., PMA, CLIA or 510(k)). Disease differentiation test reimbursement is more widespread than other PM tests because of better evidence, guidelines, and clinician preferences. Predisposition tests may be reimbursed, despite the lack of randomized clinical trials, because people may value the information from testing, regardless of the clinical consequences. Pharmacogenetics (PGx) faces reimbursement hurdles because of the lack of evidence about clinical utility, though some companies bypass payers, and market PGx tests directly to consumers. An additional challenge for all PM is the cumbersome existing coding system for reimbursement and the lack of value-based arrangements. **CONCLUSIONS:** To date, the promise and hype of PM has outpaced its evidentiary support. In order to achieve favorable coverage and reimbursement and to support premium prices for PM, manufacturers will need to bring better clinical evidence to the marketplace and develop better support for the value of their products. More flexible reimbursement systems are needed to reward PM technologies that demonstrate evidence of value.

PM2

IMPACT OF PHARMACOGENETICS ON THE COSTS OF MANAGING ADVERSE EVENTS WITH WARFARIN: A PROSPECTIVE ANALYSIS

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OBJECTIVES: The anticoagulant effect of warfarin is subject to wide dose variability that may lead to hemorrhagic and thrombotic events. Variations in the *CYP2C9* and *VKORC1* genes together with clinical factors explain approximately 50% of this variability. The aim was to estimate the health care resource use, and overall costs associated with therapy from the perspective of the UK NHS. **METHODS:** As part of a 6-month prospective cohort study evaluating pharmacogenetic and clinical factors associated with warfarin therapy, patients' use of resources were recorded and costs valued (UK ≤ for 2006/7). Resource use was compared among patient sub-groups (defined by age; gender; *CYP2C9* genotype; *VKORC1* genotype; adverse events; co-medication; co-morbidities; and smoking status). Mean costs were calculated with 95%CI estimated using non-parametric bootstrap sampling. **RESULTS:** Complete data were available for 254 patients. During the study period a total of 930 anticoagulation visits (median 3 per patient, IQR 1, 5) and 4059 INR measurements (median 15, IQR 10, 20) were recorded. Of the 70 patients who had experienced an adverse event, 16 (6.3%) required hospitalisation. Controlling for age, gender, and co-morbidities in patients who experienced an adverse event, the OR for hospitalization was 8.35

(95%CI 1.44, 48.35) for patients with the VKORC1 TT (rs9923231) genotype compared with other genotypes. The mean cost of health care attributable to warfarin therapy was ≤392. The management of warfarin-related adverse events contributed to 53% of the overall cost. The mean costs for those who experienced an adverse event was ≤884 (95%CI, 554, 1837) compared with ≤178 (95%CI, 164, 192) for the 179 patients who did not. **CONCLUSIONS:** Our analysis is the first to demonstrate a significant association between *VKORC1* variant genotype and hospitalization. Although no independent effect on total cost was evident, carriers of VKORC1 TT were eight times more likely to be hospitalized due to adverse events.

PM3

USE OF PHARMACOGENETIC TESTING TO DETERMINE ADJUVANT HORMONAL THERAPY CHOICE IN EARLY STAGE BREAST CANCER PATIENTS: A VALUE OF INFORMATION ANALYSIS

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OBJECTIVES: To estimate the uncertainty regarding adjuvant treatment selection for postmenopausal women with early stage oestrogen-receptor positive breast cancer when pre-treatment CYP2D6 pharmacogenetic testing is considered as an option. In addition, the expected value of partial perfect information (EVPPI) was estimated for different parameter sets to inform research prioritisation. **METHODS:** A decision analytic model estimated lifetime costs and quality adjusted life years (QALYs) for four comparators: 5 years of tamoxifen; 5 years of an aromatase inhibitor (AI); CYP2D6 test and treat wt/wt genotypes with tamoxifen and other genotypes with an AI; CYP2D6 test and treat wt/wt and wt/*4 genotypes with tamoxifen and *4/*4 genotypes with an AI. No trial data for CYP2D6 contingent treatment pathways were identified. Trial data comparing tamoxifen to anastrozole was therefore synthesised with observational data linking CYP2D6 genotype to recurrence in patients receiving tamoxifen. Estimates of the EVPPI were derived by attaching distributions to input parameters and using two-level Monte Carlo simulation. EVPPI estimates were generated for parameters describing the efficacy of tamoxifen and anastrozole; parameters describing genotype-specific tamoxifen efficacy; genotype prevalence; utility weights and health state costs. **RESULTS:** The strategy of CYP2D6 test and treat wt/wt patients with tamoxifen and all others with an AI maximised expected net benefit assuming a decision threshold of ≤30,000/QALY, and had an incremental cost-effectiveness ratio of ≤14,133/QALY. However, this maximised net benefit with only 61% certainty. This substantial decision uncertainty led to an expected value of perfect information estimate of ≤84 million. The EVPPI estimate for parameters describing genotype-specific tamoxifen efficacy was ≤57 million. Estimates for other parameter groups were low. **CONCLUSIONS:** Further CYP2D6 genotyping studies amongst patients receiving tamoxifen should be prioritised. Expected value of sample information analysis could be used to establish the cost-effectiveness and optimal design of this primary research.

PM4

AN EXPLORATION OF THE POTENTIAL CLINICAL BENEFITS AND RISKS OF CYP2D6 TESTING TO GUIDE TAMOXIFEN THERAPY IN BREAST CANCER

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OBJECTIVES: Recent studies have reported that women receiving adjuvant tamoxifen with CYP2D6 poor metabolizer genotype have a higher risk of breast cancer recurrence than women without poor metabolizer genotype. The objective of this study was to evaluate pharmacogenetic testing for CYP2D6 variants as an approach to help clinicians identify postmenopausal women that would be better candidates for alternative therapies. **METHODS:** We developed a decision-analytic lifetime Markov model consisting of 6 health states and assessed a hypothetical cohort of 64-year old women with ER+ breast cancer receiving tamoxifen. We assumed women who were poor metabolizers would be switched to anastrazole. The incidence of local regional relapse, metastasis, and breast cancer death were obtained from the 2005 ATAC trial. The hazard ratio for disease recurrence in poor vs. extensive metabolizers was derived from a recent study by Goetz et al. Cost, utilities and background mortality rates were obtained from the published literature or publicly available sources. One-way sensitivity analyses and scenario analyses were conducted to evaluate uncertainty. **RESULTS:** Projected disease free survival at 5 years was 81.4% for tamoxifen and 83.3% for anastrozole, compared to 81.0% and 83.8% in the ATAC trial. Treatment with tamoxifen resulted in 11.95 QALYs, anastrozole 12.15 QALYs, and CYP2D6-guided treatment 12.19 QALYs. The testing strategy resulted in the greatest QALYs with a hazard ratio for recurrence in CYP2D6 variant versus wild-type patients of 1.66 or higher, or variant prevalence greater than 20%. **CONCLUSIONS:** Genetic testing for CYP2D6 status in postmenopausal women taking adjuvant tamoxifen may lead to clinically meaningful improvements in survival and quality of life. Evaluation of the relative impact of drug-related adverse events, validation of association studies, and assessment in ethnically diverse populations are needed before widespread testing can be recommended.

PODIUM SESSION I: RESEARCH ON METHODS – Utility Methods

UT1

ON THE ISSUE OF UTILITY MULTIPLICATION: A REVISIT

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OBJECTIVE: Several estimators exist when average utility scores are not available for patient populations with multiple disease conditions. The multiplicative estimator is a widespread choice among them. This study is to empirically test the accuracy of the multiplicative estimator and compare it with other estimators. **METHODS:** Using the pooled Medical Expenditure Panel Survey (MEPS) 2001 and 2003 data, a sample of 40,846 adults with EQ-5D preference-based index scores were categorized into 238 disease condition categories. Due to the MEPS sampling property, co-morbid pair categories with less than 100 individuals were excluded, which left us with 760 co-morbid pairs in total. The study focus was the bias from the estimators to the observed mean scores for each co-morbid pair, with the observed scores presumed to be the true value. The analyses were conducted using both the raw estimators and the rescaled (purified) estimators. Regressions and concordance correlation coefficients were also used to evaluate the agreement between the estimators and the observed scores. **RESULTS:** Using the rescaled approach, the scores estimated by multiplying the 2 mean scores of the corresponding disease conditions on average had a statistically significantly larger bias ($p < 0.0001$) from the observed ones (–0.043) than simply picking the smaller mean of the 2 paired conditions (minimum estimator, bias = 0.027). However, the multiplicative estimator had less bias than other estimators including the additive estimator (bias = –0.054), the larger mean (bias = 0.077), the average of the means (bias = 0.052), mean of the condition with smaller sample (bias = 0.053). Results produced by other analyses, including using the raw scores, all favored the minimum estimator than the multiplicative estimator. **CONCLUSIONS:** Multiplication is not a good estimate when the average utility score for patients with 2 disease conditions is not readily available. The lower of the 2 utility scores had the least error among those estimators that we compared.

UT2

ELICITING TIME TRADE-OFF AMOUNTS FOR HEALTH STATES IN HYPOTHETICAL INDIVIDUALS OF DIFFERENT AGES USING A DISCRETE CHOICE EXPERIMENT

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OBJECTIVE: To measure whether public values for health vary with the age of the affected individual. **METHODS:** We fielded a discrete choice experiment via the internet in December 2007 to measure preferences for different attributes of influenza-related health states: length of episode (days of illness), severity of illness (workdays lost), age of hypothetical affected individual (range: 1–85 yrs), and time-tradeoff amounts (1day – 2 yrs). We also collected data on socio-demographic characteristics and experience with influenza illness. Respondents were 18 years and older and matched to reflect characteristics of the general US adult population (n = 1012). Response rate was 67%. Respondents were presented with pairs of illness profiles for a hypothetical individual and indicated the profile they preferred. Each respondent answered 8 discrete choice questions. A full factorial design was used. Discrete choice analysis using generalized estimating equations was used to evaluate the relative value of different attributes in the illness profile while controlling for socio-demographic characteristics and influenza experience. **RESULTS:** As measured by time-tradeoff amounts, respondents preferred shorter influenza episodes (total length) but did not significantly prefer fewer workdays lost if episode length was held constant. Respondents preferred to avert uncomplicated illness in very young children (1 year old child: odds ratio = 2.35, $p < 0.05$; 3 year old child: odds ratio = 3.21, $p < 0.01$) and older adults (85 year old: odds ratio = 2.41, $p < 0.05$) compared to a 35 year old adult. For an influenza-related hospitalization, respondents preferred to avert illness in very young children (1 year old child: odds ratio = 2.86, $p < 0.01$) compared to a 35 year old adult. **CONCLUSIONS:** Approaches that assume values for illnesses do not vary with the age of a patient may bias economic analyses that use these values. If patient age is likely to affect valuations, then age should be included as an attribute in the valuation exercise.

UT3

THE VALUE OF ADDED LIFE YEARS AS A FUNCTION OF AGE, PROGNOSIS AND QUALITY OF LIFE

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OBJECTIVE: Do people weigh gains in life years differently when patients differ in age (but not in life expectancy), life expectancy (but not in age) or QOL (but not age or life expectancy)? **METHODS:** Trade off questions wer developed searching for indifference between giving healthy life years to patients with different ages, prognoses and quality of life. Data come from 46 heart failure patients, 60 healthy controls and 180 students. For age, as well as prognosis and QOL, six comparative sets were developed. Each respondent answered two questions of each set and two combination-questions. Ordered logistic regression was used in combination with conditional linear regression for "extreme" answers. Answers are "extreme" when, for example, one extra life year in a young patient is preferred to 10 in an old patient or when respondents can't choose. **RESULTS:** More than 40% of the answers are "extreme".